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L16: Entry 8 of 33 File: USPT Oct 12, 1999

US-PAT-NO: 5965163
DOCUMENT-IDENTIFIER: US 5965163 A

TITLE: Substained release compositions and a method of preparing pharmaceutical compositions

DATE-ISSUED: October 12, 1999

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Miller; Ronald Brown	Basel	N/A	N/A	CHX
Leslie; Stewart Thomas	Cambridge	N/A	N/A	GBX
Malkowska; Sandra Therese Antoinette	Cambridge	N/A	N/A	GBX
Prater; Derek Allan	Cambridge	N/A	N/A	GBX
Knott; Trevor John	Essex	N/A	N/A	GBX
Heafield; Joanne	Cambridge	N/A	N/A	GBX
Challis; Deborah	Kent	N/A	N/A	GBX

US-CL-CURRENT: 424/468; 424/451, 424/452, 424/457, 424/464, 424/469, 424/470, 424/484, 424/485, 424/486, 424/487, 424/488, 424/489

CLAIMS:

What is claimed is:
1. A solid dosage form comprising a plurality of particles, the plurality of particles including a pharmaceutically active substance in a matrix, the matrix including a fusible material having a melting point of from 35.degree. C. to 150.degree. C. the fusible material including a mixture of a hydrophobic fusible carrier and a hydrophilic fusible carrier, wherein said particles are formed by the process of:
(a) controlling a granulation process to produce irregular shaped agglomerates;
(b) comminuting the agglomerates to provide controlled release particles in a size range of about 0.5 mm to about 2 mm;
(c) mechanically working the agglomerates.
2. The solid dosage form according to claim 1, wherein said process further comprises adding a release control component to said mixture of a hydrophobic fusible carrier and hydrophilic fusible carrier wherein said release control component is selected from the group consisting of a water soluble fusible material, a particulate organic material, a particulate inorganic material, a particulate organic material, a particulate inorganic material, and mixtures thereof.
3. The solid dosage form according to claim 1, wherein the pharmaceutically active substance is an opioid.
4. The solid dosage form according to claim 3, wherein said opioid is morphine, tramadol, hydromorphone, oxycodone, diamorphine or a pharmaceutically acceptable salt thereof.
5. The solid dosage form according to claim 1, wherein said hydrophobic fusible carrier is a material selected from the group consisting of hydrogenated vegetable oil and hydrogenated castor oil.
6. The solid dosage form according to claim 2, wherein said release control component of water-soluble fusible material is a polyethylene glycol.
7. The solid dosage form according to claim 2, wherein said release control component is selected from the group consisting of polyethylene glycol, dicalcium phosphate, calcium sulfate, talc, colloidal anhydrous silica, lactose, poloxamers,

microcrystalline cellulose, starch, hydroxypropyl-cellulose and hydroxypropylmethylcellulose.
8. The solid dosage form according to claim 1, wherein steps a and c are performed using a high speed mixer and wherein additional energy is provided to the agglomerates being mixed by the high speed mixer by microwave energy.
9. The solid dosage form according to claim 1, wherein the dosage form contains morphine sufficient to provide a plasma concentration of morphine effective to provide an analgesic effect for 24 hours after administration of said dosage form.

10. The solid dosage form according to claim 9, wherein the active substance is morphine sulfate which upon administration provides peak plasma levels of from 3.2 to 29.2 ng/ml of morphine at median times between about 2 and about 6 hours following administration.
11. The solid dosage form according to claim 1, wherein the active substance is morphine sulfate which upon administration provides a mean maximum plasma concentration (C.sub.max) of 9.2 ng/ml at a median time to reach maximum plasma concentration (T.sub.max) of said active in about 2.5 hours, and a C.sub.max of 11.9 ng/ml at median T.sub.max of about 4 hours.
12. The solid dosage form according to claim 1, wherein the hydrophobic carrier is at least 25% by weight of the total amount of ingredients added.
13. The solid dosage form according to claim 1, wherein the granulation process further comprises addition of microwave energy to the granulation mix.
14. The solid dosage form according to claim 10, wherein the hydrophobic carrier is at least 40% by weight of the total amount of ingredients added.
15. The solid dosage form according to claim 1, wherein said particles are compressed into a tablet.
16. The solid dosage form according to claim 1, wherein said particles are disposed in a capsule.
17. The solid dosage form according to claim 1, wherein step (c) is repeated from one to five times.
18. The solid dosage form of claim 1, wherein steps (b) and (c) are repeated from one to five times.
19. The solid dosage form of claim 1, wherein step (c) further includes mechanically working the agglomerates with a hydrophilic fusible carrier, a hydrophobic fusible carrier, a diluent, or mixtures thereof.
20. A solid dosage form comprising a plurality of particles the plurality of particles including a pharmaceutically active substance in a matrix the matrix including a hydrophobic fusible carrier having a melting point of from 35.degree. C. to 150.degree. C. selected from the group consisting of a hydrogenated vegetable oil, castor oil, and mixtures thereof wherein said particles are formed by the process of:
(a) controlling a granulation process to produce irregular shaped agglomerates;
(b) comminuting the agglomerates to provide controlled release particles in a size range of about 0.5 to about 2 mm;
(c) mechanically working the agglomerates.
21. The solid dosage form according to claim 20, wherein said process further comprises adding particulate fusible material in the amount of between 5% and 75% w/w to said irregular-shaped agglomerates and mechanically working said irregular shaped agglomerates and said particulate fusible material.
22. The solid dosage form according to claim 20, further comprising a hydrophilic carrier.
23. The solid dosage form of claim 20, wherein step (c) is repeated from one to five times.
24. The solid dosage form of claim 20, wherein steps (b) and (c) are repeated from one to five times.
25. The solid dosage form of claim 20, wherein step (c) further includes mechanically working the agglomerates with a hydrophilic fusible carrier, a hydrophobic fusible carrier, a diluent, or mixtures thereof.
26. A solid dosage form comprising a plurality of particles, the plurality of particles including a pharmaceutically active substance selected from the group consisting of morphine, tramadol, hydromorphone, oxycodone, diamorphine, and pharmaceutically acceptable salts thereof, in a matrix, the matrix including a fusible material having a melting point of from 35.degree. C. to 150.degree. C., the fusible material including a mixture of a hydrophobic fusible carrier and a hydrophilic fusible carrier, wherein said particles are formed by the process of:
(a) controlling a granulation process to produce irregular shaped agglomerates;
(b) comminuting the agglomerates to provide controlled release particles in a size range of about 0.5 mm to about 2 mm;
(c) mechanically working the agglomerates.

27. The solid dosage form according to claim 26, wherein step (c) is repeated from one to five times.
28. The solid dosage form of claim 26, wherein steps (b) and (c) are repeated from one to five times.
29. The solid dosage form of claim 26, wherein step (c) further includes mechanically working the agglomerates with a hydrophilic fusible carrier, a hydrophobic fusible carrier, a diluent, or mixtures thereof.
30. A solid dosage form comprising a plurality of particles, the plurality of particles including a pharmaceutically active substance selected from the group consisting of morphine, tramadol, hydromorphone, oxycodone, diamorphine, and pharmaceutically acceptable salts thereof, in a matrix, the matrix including a hydrophobic fusible carrier having a melting point of from 35.degree. C. to 150.degree. C., the hydrophobic fusible carrier selected from the group consisting of a hydrogenated vegetable oil, castor oil, and mixtures thereof, wherein said particles are formed by the process of:
(a) controlling a granulation process to produce irregular shaped agglomerates;
(b) comminuting the agglomerates to provide controlled release particles in a size range of about 0.5 to about 2 mm;
(c) mechanically working the agglomerates.
31. The solid dosage form according to claim 30, wherein step (c) is repeated from one to five times.
32. The solid dosage form of claim 30, wherein steps (b) and (c) are repeated from one to five times.
33. The solid dosage form of claim 30, wherein step (c) further includes mechanically working the agglomerates with a hydrophilic fusible carrier, a hydrophobic fusible carrier, a diluent, or mixtures thereof.

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L19: Entry 1 of 2 File: USPT Jul 27, 1993

DOCUMENT-IDENTIFIER: US 5231089 A
TITLE: Method of improving oral bioavailability of carbamazepine

BSPR:
CIBA-GEIGY AG's European Patent Publication No. 0435826, published Jul. 3, 1991, describes an aqueous intravenous solution of carbamazepine or oxcarbazepine for use in treating status epilepticus. The aqueous solubility of the drug is enhanced by means of a hydrophilic C.sub.1 -C.sub.6 alkyl, carboxy C.sub.1 -C.sub.6 alkyl, C.sub.1 -C.sub.6 alkoxycarbonyl C.sub.1 -C.sub.6 alkyl and/or hydroxy C.sub.2 -C.sub.6 alkyl .gamma.-cyclodextrin derivative. 2-Hydroxypropyl-, 3-hydroxypropyl- and 2-hydroxyethyl-.gamma.-cyclodextrin are specifically disclosed.

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L13: Entry 9 of 15 File: USPT Nov 19, 1991

US-PAT-NO: 5066441
DOCUMENT-IDENTIFIER: US 5066441 A

TITLE: Process for compacting a calcium phosphate composition

DATE-ISSUED: November 19, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gerard; Thomas W.	Upper Saddle River	NJ	N/A	N/A

US-CL-CURRENT: 264/118; 23/293R, 264/109, 264/175, 423/311, 424/602

CLAIMS:

I claim:
1. A mechanical process for treating calcium phosphate fine particles comprising compacting dry-mixed fine particles consisting essentially of calcium phosphate under pressure to form compacted calcium phosphate and comminuting the compacted calcium phosphate to granules suitable for use as an excipient for making pharmaceutical tablets.
2. The process described in claim 1 wherein the calcium phosphate is selected from the group consisting of dicalcium phosphate dihydrate, tricalcium phosphate, and calcium pyrophosphate.
3. The process described in claim 1 wherein the calcium phosphate is anhydrous monocalcium phosphate.
4. The process described in claim 1 wherein the calcium phosphate is monocalcium phosphate monohydrate.
5. The process described in claim 1 wherein the calcium phosphate is anhydrous dicalcium phosphate.
6. The process described in claim 1 wherein the calcium phosphate is tricalcium phosphate.
7. A mechanical process for treating fine particles consisting essentially of drymixed calcium phosphate which includes the step of compacting the particles under pressure to form a compacted calcium phosphate followed by the additional step of comminuting said compacted calcium phosphate to granules.
8. A mechanical process for treating fine particles consisting essentially of drymixed calcium phosphate which includes the step of compacting the particles under pressure to form a compacted calcium phosphate wherein the pressure ranges from about 4,000 to about 18,000 lbs. force per linear inch of roll width in a roller compactor.
9. A mechanical process for treating fine particles consisting essentially of drymixed calcium phosphate which includes the step of compacting the particles under pressure to form a compacted calcium phosphate wherein the pressure ranges from about 8,000 to about 14,000 lbs. force per linear inch of roll width in a roller compactor.
10. An improved mechanical process for forming granules from fine particles of calcium phosphate of less than 75 microns comprising compacting in a roller compactor particles consisting essentially of dry mixed calcium phosphate having a particle size of less than about 75 microns under pressure sufficient to form compacted calcium phosphate and comminuting said compacted calcium phosphate to form granules of a particle size larger than 75 microns.

L13: Entry 7 of 15 File: USPT May 10, 1994

US-PAT-NO: 5310734
DOCUMENT-IDENTIFIER: US 5310734 A

TITLE: Phospholipid composition

DATE-ISSUED: May 10, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Losch; Rainer	Bonn	N/A	N/A	DEX
Gunther; Bernd-Rainer	Bergheim	N/A	N/A	DEX
Hager; Jorg	Cologne	N/A	N/A	DEX

US-CL-CURRENT: 514/78; 424/439

CLAIMS:

We claim:
1. A process for the manufacture of a granulated phospholipid composition comprising
cooling a phospholipid starting material having a phosphatidylcholine content of at least 80% by weight and is substantially free from additives to a temperature below -50.degree. C., and
comminuting said cooled phospholipid starting material until it has a particle size between 18 mm and 0.07 mm.
2. The process of claim 1 comprising comminuting said phospholipid starting material until it has a particle size between 6 mm and 0.5 mm.
3. The process of claim 1 further comprising storing said phospholipid starting material at a temperature between +5.degree. C. and -60.degree. C. before said comminuting step.
4. The process of claim 3 wherein said phospholipid starting material is stored or between one and 150 days before said comminuting step.
5. The process of claim 3 wherein said phospholipid starting material is stored for between one and 70 days before said comminuting step.
6. The process of claim 1 wherein said comminuting step is carried out under an inert gas.
7. The process of claim 3 wherein said storing step is carried out under an inert gas.
8. The process of claim 7 wherein said inert gas is nitrogen, carbon dioxide, a noble gas or a mixture thereof.
9. The processor of claim 3 further comprising warming said phospholipid starting material to room temperature after said storing step and before said comminuting step.
10. The process of claim 1 further comprising storing said phospholipid starting material at a temperature between -10.degree. C. and -30.degree. C. before said comminuting step.
11. The process of claim 1 wherein said phospholipid starting material is isolated from soy lecithin and contains 93.+-.3% by weight phosphatidylcholine.
12. The process of claim 1 further comprising storing said phospholipid composition at a temperature of <10.degree. C.
13. The process of claim 1 further comprising storing said phospholipid composition at a temperature of between 1.degree. C. and 6.degree. C.
14. The process of claim 13 wherein said phospholipid composition is stored under an inert gas.

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L13: Entry 11 of 15 File: USPT May 23, 1989

US-PAT-NO: 4832956
DOCUMENT-IDENTIFIER: US 4832956 A

TITLE: Disintegrating tablet and process for its preparation

DATE-ISSUED: May 23, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Gergely; Gerhard	Vienna, A-1050	N/A	N/A	ATX
Gergely; Thomas	Vienna, A-1050	N/A	N/A	ATX
Gergely; Irmgard	Vienna, A-1050	N/A	N/A	ATX

US-CL-CURRENT: 424/466; 424/468, 424/479, 424/480, 424/482

CLAIMS:

We claim:
1. A tablet comprising at least one slowly or sparingly soluble pharmaceutically active compound, an effective amount of at least one disintegrating agent which disintegrates upon contact with water, and the balance comprising primarily at lest one soluble filler in a form which renders it more slowly soluble on contact with water than the disintegrating action of said disintegrating agent.
2. A tablet as claimed in claim 1, wherein the filler comprises a melt which has been comminuted into filler particles having a size of about 0.1 to 0.6 mm.
3. A tablet as claimed in claim 2, wherein the filler particles comprise at least one of the substances mannitol, orbitol and xylitol.
4. A tablet as claimed in claim 2, wherein the filler particles comprise at least one of the substances citric acid and adipic acid.
5. A tablet as claimed in claim 2, wherein the filler particles incorporate therein at least one pharmaceutically active compound.
6. A tablet as claimed in claim 2, the filler particles incorporate therein at least one disintegrating agent.
7. A tablet as claimed in claim 2, wherein the filler particles incorporate therein at least one material selected from the group consisting of another type of filler, a disintegrating agent, a pharmaceutically active compound and an auxiliary compound.
8. A tablet as claimed in claim 2, wherein, in addition to the active compound, the disintegrating agent and the filler, the tablet further comprises about 20% to about 331/3% by weight of readily soluble auxiliaries based on the total amount.
9. A multilayer tablet comprising at least one layer having a composition according to claim 2 wherein said tablet further comprises an effervescent layer.
10. A tablet as claimed in claim 2 wherein said filler comprises a carbohydrate.
11. A tablet as claimed in claim 2 wherein said disintegrating agent is selected from the group consisting of starch, silica, microcellulose, and polyvinylpyrrolidone.
12. A tablet as claimed in claim 1, wherein the filler comprises a melt.
13. The tablet of claim 2, wherein said melt has been comminuted into filler particles of a predetermined size.
14. A tablet as claimed in claim 3, wherein said filler particles have a size of about 0.1 to 0.6 nm.
15. A tablet as claimed in claim 1, wherein said soluble filler is coated with a layer of a slow dissolving material.
16. A tablet comprising a therapeutically effective amount o at least one slowly or sparingly soluble pharmaceutically active compound, an effective amount of at

least one disintegrating agent, and the balance comprising primarily granules of a fused filler material, said filler material being selected from the group consisting of mannitol, sorbitol, xylitol, and combinations thereof, said disintegrating agent being dispersed within said granules.

17. A process for the preparation of a tablet, comprising melting a filler material, dispersing an effective amount of at least one disintegrating agent in said melt, cooling said melt, comminuting said cooled melt into granules of a predetermined particle size, admixing a therapeutically effective amount of a slowly or sparingly soluble pharmaceutically active compound with said granules, and pressing said mixture into tablet form.

18. Process as claimed in claim 17, wherein at least one compound selected from the group consisting of another type of disintegrating agent, a pharmaceutically active compound and an auxiliary compound is also dispersed in the melt.

19. Process as claimed in claim 17, wherein at least one compound selected from the group consisting of a pharmaceutically active compound, an auxiliary compound and another type of disintegrating agent is admixed to said particles before pressing into a tablet.

End of Result Set

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L13: Entry 15 of 15 File: USPT Dec 14, 1971

US-PAT-NO: 3627583
DOCUMENT-IDENTIFIER: US 3627583 A

TITLE: DIRECT COMPRESSION VEHICLES

DATE-ISSUED: December 14, 1971

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Troy; John P.	Hicksville	NY	N/A	N/A
Monti; Anthony	Irvington	NY	N/A	N/A
Lynch; Frank J.	Staten Island	NY	N/A	N/A
Broeg; Charles B.	Short Hills	NJ	N/A	N/A

US-CL-CURRENT: 127/29; 127/63, 424/606, 424/686, 424/687, 424/690, 424/695, 424/720, 424/722, 424/723, 426/285, 426/453 , 426/539, 426/548, 426/590, 426/650, 514/772

CLAIMS:

What is claimed is:
1. A method for preparing tablets containing as a direct compression vehicle a sugar composition comprising the steps of (a) forming a uniform nongranulated mixture of an active material and a dry, free-flowing, generally spherical, porous agglomerate of 100 parts of a solid pulverized sugar in 0.1 to about 30 parts of a matrix of a polyhydroxy compound, and (b) compressing said mixture into tablets, said agglomerate comprising at least 10 percent of said mixture, and having a particle size of from about 12 to about 325 mesh, a moisture content of from about 0.1 to about 3 percent, and having been prepared by a process including the steps of: (1) Spraying a particulate solid sugar with an aqueous solution of binder; (2) Providing the resulting mixture with sufficient high intensity agitation to uniformly intermingle the sugar and binder and to build up agglomerates of a desired size; and (3) "Snowballing" the agglomerates to impart a general spherical shape thereto and to firm or densify the agglomerate.
2. A tablet prepared in accordance with claim 1.
3. A method according to claim 1, wherein said matrix is a carbohydrate.
4. A tablet prepared in accordance with claim 3.
5. A method according to claim 3, wherein said sugar is sucrose and said carbohydrate is invert sugar.
6. A tablet prepared in accordance with claim 5.
7. A method for preparing a direct compression vehicle comprising compacting a dry, free-flowing, generally spherical, porous agglomerate of 100 parts of a solid pulverized sugar in 0.1 to 30 parts of a matrix of a polyhydroxy compound, said agglomerate having a particle size of from about 12 to about 325 mesh and a moisture content of from about 0.1 to about 3 percent, said agglomerate being prepared by a process including the steps of:
1. Spraying a particulate solid sugar with an aqueous solution of binder;
2. Providing the resulting mixture with sufficient high intensity agitation to uniformly intermingle the sugar and binder and to build up agglomerates of a desired size; and
3. "Snowballing" the agglomerates to impart a general spherical shape thereto and to firm or densify the agglomerate,
and thereafter comminuting said compacted agglomerate to a desired particle size.
8. The product of claim 7.

8. The product of claim 7.
9. A method for preparing a tablet comprising forming a uniform admixture of the product of claim 8 and an active material, said product comprising at least 10 percent of said mixture, and compressing the mixture into tablets.
10. A tablet produced according to claim 9.

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L20: Entry 1 of 2 File: USPT May 25, 1999

DOCUMENT-IDENTIFIER: US 5906832 A
TITLE: Method for treating epilepsies

CLPR:
1. A method for the continuous administration of an antiepileptic drug to the gastrointestinal tract of a human, wherein the method comprises: (a) admitting orally into the gastrointestinal tract of the human an osmotic dosage form that maintains its integrity in the gastrointestinal tract, comprising: a composition comprising: 0.5 wt % to 90 wt % of an antiepileptic drug selected from the group consisting of phenytoin, mephenytoin, phenobarbital, primidone, carbamazepine, ethosuximide, methsuximide, phensuximide, trimethadione, clonazipam, clorazepate, phenacemide, paramethadione, primaclone, clobazam, felbamate, flunarizine, lamotrigine, progabide, vibabatim, eterobarb, gabapentin, oxcarbazepine, ralitoline, tiagobine, sulthiame, and tioridone; 10 wt % to 75 wt % of a dispensing polymer compatible with the antiepileptic drug that aids in delivering the antiepileptic drug in a therapeutic dose from the dosage form; and 0 wt % to 10 wt % of a pharmaceutically acceptable surfactant; with the total weight of all ingredients in the composition equal to 100 wt % which composition is surrounded by a subcoat comprising a nontoxic, nonionic polymer that prevents the antiepileptic drug from converting from a soluble to an insoluble antiepileptic drug in the gastrointestinal pH: a wall permeable to fluid and impermeable to an antiepileptic drug that surrounds the subcoat; and, an exit in the wall for delivering the antiepileptic drug from the dosage form; and, (b) administering the antiepileptic drug from the dosage form to the human over an extended period of time by continuous release in a therapeutically responsive dose to provide antiepileptic therapy for the human.

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L25: Entry 2 of 3 File: USPT Aug 19, 1997

DOCUMENT-IDENTIFIER: US 5658900 A
TITLE: Application of carbamazepine and oxcarbazepine in the treatment of Parkinson's disease and parkinsonian syndromes

DEPR:
As liquid compositions for oral administration, pharmaceutically acceptable solutions, suspensions, emulsions, syrups and elixirs may be used, containing inert diluents such as water, ethanol, glycerol, vegetable oils or liquid paraffin. These compositions can comprise substances other than diluents, for example wetting, sweetening, thickening, flavouring or stabilizing products.

DEPR:
The sterile compositions for parenteral administration can preferably be solutions, aqueous or non-aqueous, suspensions or emulsions. As a solvent or vehicle, water, propylene glycol, a polyethylene glycol, vegetable oils, especially olive oil, injectable organic esters, for example ethyl oleate, or other suitable organic solvents may be employed. These compositions can also contain adjuvants, especially wetting, tonicity, emulsifying, dispersing and stabilizing agents. The sterilization may be carried out in several ways, for example by aseptic filtration, by incorporation of sterilizing agents in the composition, by irradiation or by heating. They may also be prepared in the form of sterile solid compositions which can be dissolved at the time of use in sterile water or any other sterile injectable medium.

DETL:
_____ Active product 10 mg Benzoic acid 80 mg Benzyl alcohol 0.06 cm.sup.3 Sodium benzoate 80 mg Ethanol, 95% 0.4 cm.sup.3 Sodium hydroxide 24 mg Propylene glycol 1.6 cm.sup.3 Water q.s. 4 cm.sup.3